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(FILE 'HOME' ENTERED AT 12:53:51 ON 31 MAR 2003)

FILE 'CAPLUS' ENTERED AT 12:54:02 ON 31 MAR 2003
L1 2212 S IN SILICO
L2 3 S L1 AND ((PROTEIN OR PEPTIDE) AND (REDUCE? IMMUNOGEN?))
L3 0 S L1 AND ((PROTEIN OR PEPTIDE) AND (IMMUNOGENECITY))
L4 8 S L1 AND ((PROTEIN OR PEPTIDE) AND (IMMUNOGEN?))
L5 5 S L4 NOT L2

=> d l4 bib,abs 1-8

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:908189 CAPLUS
DN 138:185948
TI Search for potential vaccine candidate open reading frames in the Bacillus anthracis virulence plasmid pXO1: in **silico** and in vitro screening
AU Ariel, N.; Zvi, A.; Grosfeld, H.; Gat, O.; Inbar, Y.; Velan, B.; Cohen, S.; Shafferman, A.
CS Department of Biochemistry and Molecular Genetics, Israel Institute for Biological Research, Ness Ziona, 74100, Israel
SO Infection and Immunity (2002), 70(12), 6817-6827
CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB A genomic anal. of the Bacillus anthracis virulence plasmid pXO1, aimed at identifying potential vaccine candidates and virulence-related genes, was carried out. The 143 previously defined open reading frames (ORFs) were subjected to extensive sequence similarity searches (with the nonredundant and unfinished microbial genome databases), as well as motif, cellular location, and domain analyses. A comparative genomics anal. was conducted with the related genomes of Bacillus subtilis, Bacillus halodurans, and Bacillus cereus and the pBtoxis plasmid of Bacillus thuringiensis var. israeliensis. As a result, the percentage of ORFs with clues about their functions increased from .apprx.30% (as previously reported) to more than 60%. The bioinformatics anal. permitted identification of novel genes with putative relevance for pathogenesis and virulence. Based on our analyses, 11 putative **proteins** were chosen as targets for functional genomics studies. A rapid and efficient functional screening method was developed, in which PCR-amplified full-length linear DNA products of the selected ORFs were transcribed and directly translated in vitro and their **immunogenicities** were assessed on the basis of their reactivities with hyperimmune anti-B. anthracis antisera. Of the 11 ORFs selected for anal., 9 were successfully expressed as full-length polypeptides, and 3 of these were found to be antigenic and to have **immunogenic** potential. The latter ORFs are currently being evaluated to det. their vaccine potential.
RE.CNT 69 THERE ARE 69 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:889930 CAPLUS
TI Rationally engineered **proteins** or antibodies with absent or reduced **immunogenicity**
AU Tangri, S.; LiCalsi, C.; Sidney, J.; Sette, A.
CS Epimmune Incorporated, San Diego, CA, 92121, USA
SO Current Medicinal Chemistry (2002), 9(24), 2191-2199
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers
DT Journal
LA English

AB One challenge assocd. with the clin. use of **protein** therapeutics destined for chronic administration is the potential for the development of unwanted anti-drug immune reactions. The mol. basis for this reactivity is the binding of **peptide** fragments (epitopes) derived from the breakdown of the **protein** drug to the HLA receptors expressed by the patient's immune cells. If these epitopes are recognized as "foreign" by the immune system, specific helper T lymphocytes (HTL), are activated, which initiate and direct the formation of antibodies against the **protein** drug. These antibodies can bind and neutralize the **protein** drug, resulting in either decreased efficacy or total ineffectiveness of the drug. Moreover, various safety concerns, such as allergic reactions and other adverse events, are also frequently assocd. with the formation of anti-drug antibodies. Herein, we describe the development of "ImmunoStealth", an integrated bioinformatics, biochem. and cellular immunol. approach that specifically addresses the issue of unwanted immune responses against **protein** therapeutics. Unwanted HTL epitopes are identified using in **silico** sequence anal. methods and high throughput in vitro biochem. evaluations and thereafter confirmed using cellular **immunogenicity** assays. The "offending" epitopes within the drug are then rationally modified to alter their HLA binding capacity, and thus render them non-recognizable by the immune system. This technol. will ultimately facilitate the design of safer, more potent and more economical drugs.

RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:832831 CAPLUS
DN 137:351519
TI Modified human interferon .alpha. with reduced **immunogenicity** for therapeutic uses
IN Carr, Francis J.; Carter, Graham; Jones, Tim; Baker, Matthew; Watkins, John; Hanlon, Marian
PA Merck Patent G.m.b.H., Germany
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002085941	A2	20021031	WO 2002-EP2218	20020301

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2001-105088 A 20010302

AB The present invention relates to polypeptides to be administered esp. to humans and in particular for therapeutic use. The polypeptides are modified polypeptides whereby the modification results in a reduced propensity for the polypeptide to elicit an immune response upon administration to the human subject. The invention in particular to the modification of human interferon alpha and specifically interferon .alpha. 2 (INF.alpha.2) to result in **proteins** that are substantially non-**immunogenic** or less **immunogenic** than any non-modified counterpart when use in vivo.

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:814284 CAPLUS
DN 137:309486
TI Surface **proteins** and their genes of Streptococcus pyogenes and their use for treatment of infections caused by .beta.-hemolytic streptococci
IN Olmstead, Stephen Bruce; Zagursky, Robert John; Nickbarg, Elliott Bruce; Winter, Laurie Anne
PA Wyeth, John and Brother Ltd., USA
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083859	A2	20021024	WO 2002-US11610	20020412

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-283358P P 20010413
AB The present invention provides nucleic acid and **protein** compns. and methods to ameliorate and prevent infections caused by all .beta.-hemolytic streptococci, including groups A, B, C, and G. To identify polynucleotides and polypeptides useful for the amelioration and prevention of infections caused by .beta.-hemolytic streptococci, two strategies, a genomic approach and a proteomic approach, were used to identify surface-localized Streptococcus pyogenes **proteins**. The genomic approach included an extensive genomic anal. in **silico** of the S. pyogenes genome using several algorithms design to identify and characterize genes that would encode surface-localized **proteins**. Some of the **proteins** are also characterized for opsonphagocytic activity. The polynucleotides, polypeptides, and antibodies of the invention can be formulated for use as **immunogenic** compns. Also disclosed are methods for immunizing against and reducing .beta.-hemolytic streptococcal infection, and for detecting .beta.-hemolytic streptococci in a biol. sample. The present invention claims a total of 668 sequences, but the Sequence Listing was not made available on publication of this patent application.

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2002:696124 CAPLUS
DN 137:226946
TI Modified ciliary neurotrophic factor (CNTF) with reduced **immunogenicity** by removing its T cell epitopes
IN Carr, Francis J.; Carter, Graham
PA Merck Patent Gmbh, Germany
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002070698	A2	20020912	WO 2002-EP2084	20020227

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI EP 2001-105089 A 20010302

AB The present invention relates to polypeptides to be administered esp. to humans and in particular for therapeutic use. The polypeptides are modified polypeptides whereby the modification results in a reduced propensity for the polypeptide to elicit an immune response upon administration to the human subject. The invention in particular relates to the modification of human ciliary neurotrophic factor (CNTF) to result in CNTF **proteins** that are substantially non-**immunogenic** or less **immunogenic** than any non-modified counterpart when used in vivo. 81 13-Amino acid T cell epitopes of human CNTF are identified and subjected to modification assisted by in **silico** modeling techniques to reduce or remove nos. of potential T-cell epitopes in CNTF for drug design. Various amino acid residues for substituting the crit. residues in these T cell epitopes are listed. DNA sequences coding for the modified **proteins**, pharmaceutical compns. contg. the modified **proteins**, and a method of manuf. of the **proteins** are also claimed but NOT provided.

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2001:785109 CAPLUS
DN 136:322902
TI T-helper cell-response to MHC class II-binding **peptides** of the renal cell carcinoma-associated antigen RAGE-1
AU Stassar, Marike J. J. G.; Raddrizzani, Laura; Hammer, Jurgen; Zoller, Margot
CS Department of Tumor Progression and Immune Defense, German Cancer Research Center (DKFZ), Heidelberg, Germany
SO Immunobiology (2001), 203(5), 743-755
CODEN: IMMND4; ISSN: 0171-2985
PB Urban & Fischer Verlag
DT Journal
LA English

AB Recently, epitope prediction software for HLA-DR binding sequences has become available. In view of the importance of T helper (Th) cell activation in immunotherapy of cancer and evidences supporting **immunogenicity** of renal cell carcinoma (RCC), we have tested 4 **peptides** of RAGE-1 binding promiscuously to HLA-DR mols. for induction of an immune response. The **peptides** predicted by the TEPITOPE program using a stringent threshold were derived from the open reading frame 2 and 5 of RAGE-1. Induction of response was evaluated by culturing peripheral blood mononuclear cells (PBMC) in the presence of **peptide**-loaded dendritic cells (DC) to det. proliferative activity and cytokine expression. Two out of 5 donors did not respond to any of the 4 **peptides**, 2 donors responded to one **peptide** and one donor responded to two other **peptides**. Notably, as revealed by blocking studies and T cell subtype definition, **peptides** bound to MHC class II mols. and **peptide** pulsed DC exclusively activated CD4+ T cells, which were of the Th1 subtype. With respect to clin. application it is important that (un)responsiveness of individual donors' PBMC was a very consistent feature. Though we have not tested explicitly whether these **peptides** correspond to naturally processed **peptides**, the possibility to define those patients whose Th might respond to in **silico** predicted **peptides** of RAGE-1, by an in vitro assay, could well be a helpful step towards setting up a RAGE-1 based immunotherapeutic protocol.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2001:209260 CAPLUS
DN 135:342702
TI HLAMatchmaker: a molecularly based donor selection algorithm for highly alloimmunized patients
AU Duquesnoy, R. J.
CS CLSI Tissue Typing Laboratory, Division of Transplantation Pathology, University of Pittsburgh Medical Center, Thomas E. Starzl Transplantation Institute, Pittsburgh, PA, USA
SO Transplantation Proceedings (2001), 33(1-2), 493-497
CODEN: TRPPA8; ISSN: 0041-1345
PB Elsevier Science Inc.
DT Journal; General Review
LA English
AB A review with refs., describes an alternative strategy for identifying potential donors for highly sensitized patients. HLAMatchmaker is an easy-to-use computer-based algorithm that addresses amino acid sequence polymorphism as crit. components of **immunogenic** epitopes that can elicit alloantibodies. This "in **silico**" compatibility test allows detn. of the structural basis of an HLA antigen mismatch. The review also discusses amino acid triplet polymorphisms in antibody-accessible sites of HLA class I mols.; detn. of HLA compatibility at the amino acid triplet level; anal. of serum reactivity patterns and identification of acceptable HLA antigen mismatches; and relative **immunogenicity** of HLA triplets.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
AN 2000:525163 CAPLUS
DN 133:236572
TI Characterization of a monoclonal antibody, D73H, that maps to a highly conserved region on fibrinogen B.beta. chain
AU Rybarczyk, B. J.; Pereira, M.; Simpson-Haidaris, P. J.
CS Department of Pathology, Medicine-Vascular, University of Rochester School of Medicine and Dentistry, Rochester, NY, USA
SO Thrombosis and Haemostasis (2000), 84(1), 43-48
CODEN: THHADQ; ISSN: 0340-6245
PB F. K. Schattauer Verlagsgesellschaft mbH
DT Journal
LA English
AB The primary structure of fibrinogen is highly conserved across species, yet often times monoclonal antibodies produced against the fibrinogen of one species will not crossreact with the fibrinogen of another. Herein, the authors describe the prodn. and characterization of murine MAb, D73H, raised against human fibrinogen. D73H cross-reacts with a highly conserved epitope on the B.beta. chain of fibrinogen from human, rat, bovine, guinea pig, and mouse. Western blotting revealed that D73H reacted with the B.beta. chain of plasmin fragment D, localizing its epitope to B.beta.134-461. A 7 kDa band was identified by D73H in Western blots of reduced fibrinogen CNBr-fragments. N-terminal sequencing mapped this fragment to B.beta.243-253, further localizing the epitope to B.beta.243-305. In **silico** anal. indicated that B.beta.243-305 is predominantly hydrophilic, and surface probability prediction indicated three potential antigenic determinants corresponding to B.beta.252-258, B.beta.262-269, and B.beta.279-286. Further in **silico** anal. of the crystal structure of fibrinogen fragment D-D indicated that B.beta.262-269 (FGRKWDPY) is predominantly .alpha.-helical and located on the surface of the mol. adjacent to a bend imposed in the .beta. chain at residue 260, which is near the junction between the rigid coiled-coil domain and the globular C-terminus. A synthetic **peptide** corresponding to B.beta.261-272 competitively inhibited the binding of D73H to the B.beta. chain of denatured intact fibrinogen and reduced and denatured B.beta. chain in Western blots, exptl. proving the validity of

these predictive algorithms. Together these data indicate that, although plasmin resistant, B.beta. chain residues B.beta.261-272 comprising the D73H epitope are highly conserved across species, surface exposed, and **immunogenic**.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT